AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph at page 7 lines 20-26 with the following:

A perfusion culture setup was developed for the PER.C6® cell line, a human cell line that possesses a number of features that makes it favourable for the production of biopharmaceuticals. A perfusion setup involves the separation of various components of the culture broth so that cells are retained, harvest is captured and medium refreshment occurs. The performance of a spinfilter, an acoustic device and an alternating tangential flow ~~Alternating Tangential Flow (ATF)~~ unit within a continuous perfusion culture of the PER.C6® cell line was assessed.

Please replace the paragraph at page 8 lines 11-18 with the following:

Cell Retention: Cells were retained in the reactor using three different devices. First a spinfilter with a 10µm pore size (GKD, Düren Germany) was used. Secondly, a Biosep ADI1015 cell retention system and controller (AppliSens, the Netherlands) was used. Finally an ATF™-4 control unit and housing with associate hollow fiber membrane module (Refine Technology, USA) was assessed. The hollow fiber filter used was model CFP-2-E-8SIP (0.2 micron, Area: 4600cm^2, Amersham Bioscience obtained from Magellan instruments, USA). To maintain a constant culture volume a level sensor control loop was in operation.

Please replace the paragraph at page 9 lines 20-25 with the following:

Figure 3: Growth of IgG1 producing PER.C6® cells in a continuous perfusion system with an ATF™-4 unit as a cell retention system. The experiment was performed in a 4L Applikon fermenter. Setting for the stirrer speed was 125 rpm. The ATF-4 operated between 0.5 and 3 working volumes per day. The SPR was set at 0.03-0.08 nL/cell/day. The inset shows the high cell density of the culture, being completely devoid of aggregating cells.

Please replace the paragraph at page 9 lines 31-32 with the following:

Figure 6: Productivity of IgG1 producing PER.C6® cells in a continuous perfusion system with an alternating tangential flow ~~ATF~~ unit as a cell retention system.

Please replace the paragraph at page 2 lines 2-5, and Table 1 with the following:

Table 1. Overview of the viable cell density, volumetric production rate (based on reactor volume) and the yield improvement of the perfusion runs using the three different retention devices. Batch and fed-batch results are added for comparison (data not shown).

Process	Max. Viable Cell Density (10^6 cells/mL)	Productivity	Yield (total amount of product produced) Improvement Factor
Batch	8-10	0.5 g/L	1
Fed-Batch	8-10	1.2 g/L	2.4
Continuous Perfusion			
Spin filter retention device	20-30	0.1-0.2 g/L/day	2.8-5.6
Acoustic retention device	20	0.6 g/L/day	16.8
Alternating tangential flow ~~ATF~~ retention device	100	0.9 g/L/day	25.2

Please replace the paragraph at page 10, lines 6-9 with the following:

It can be concluded that continuous perfusion experiments using the alternating tangential flow ~~ATF~~ unit show significant potential to achieve very high cell densities and product concentrations ($100x10^6$ cells/mL and 0.9 g/L/day), while no aggregation of the PER.C6® cells was observed.

Please replace the paragraph at page 10, lines 13-16 with the following:

Equipment: B.Braun fermenter control unit (Braun, Germany), 7L Braun vessel and

headplate with associated pH, dissolved oxygen (DO) and level sensor probes (Braun, Germany), ATF™-4 control unit and housing with associate hollow fiber membrane module (Refine Technology, USA).

Please replace the paragraph at page 11, lines 5 with the following

Alternating tangential flow ~~ATF~~ settings